

REGIOSPECIFIC REACTIONS OF PHENOL SALTS: REACTION-PATHWAYS OF ALKYLPHENOXY-MAGNESIUMHALIDES WITH TRIETHYLORTHOFORMATE

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It is known that phenols react with alkyl orthoformates and other orthoesters (ortho acetates, ortho propionates, etc.) giving alkylaryl ethers, alkylaryl ortho esters or aryl ortho esters, with exclusive attack at the oxygen atom.^{1,2}

We have found that particular phenol salts,³ such as magnesium halides, react with triethyl orthoformate giving a C-regiospecific⁴ attack at the *ortho*-position to the phenoxy group.

The reaction is quite complex and, depending upon the phenol and the reaction conditions, produces 2-hydroxyaryl-1-carboxyaldehyde diethylacetals (II), 2,2'-dihydroxyarylmethyl-ethylethers (III), 2,2',2"-trihydroxytriphenylmethanes (IV), 2,2'-dihydroxydiphenylmethanes (V), arylxantenes (VII), and xantenes (VIII). (See scheme and table).

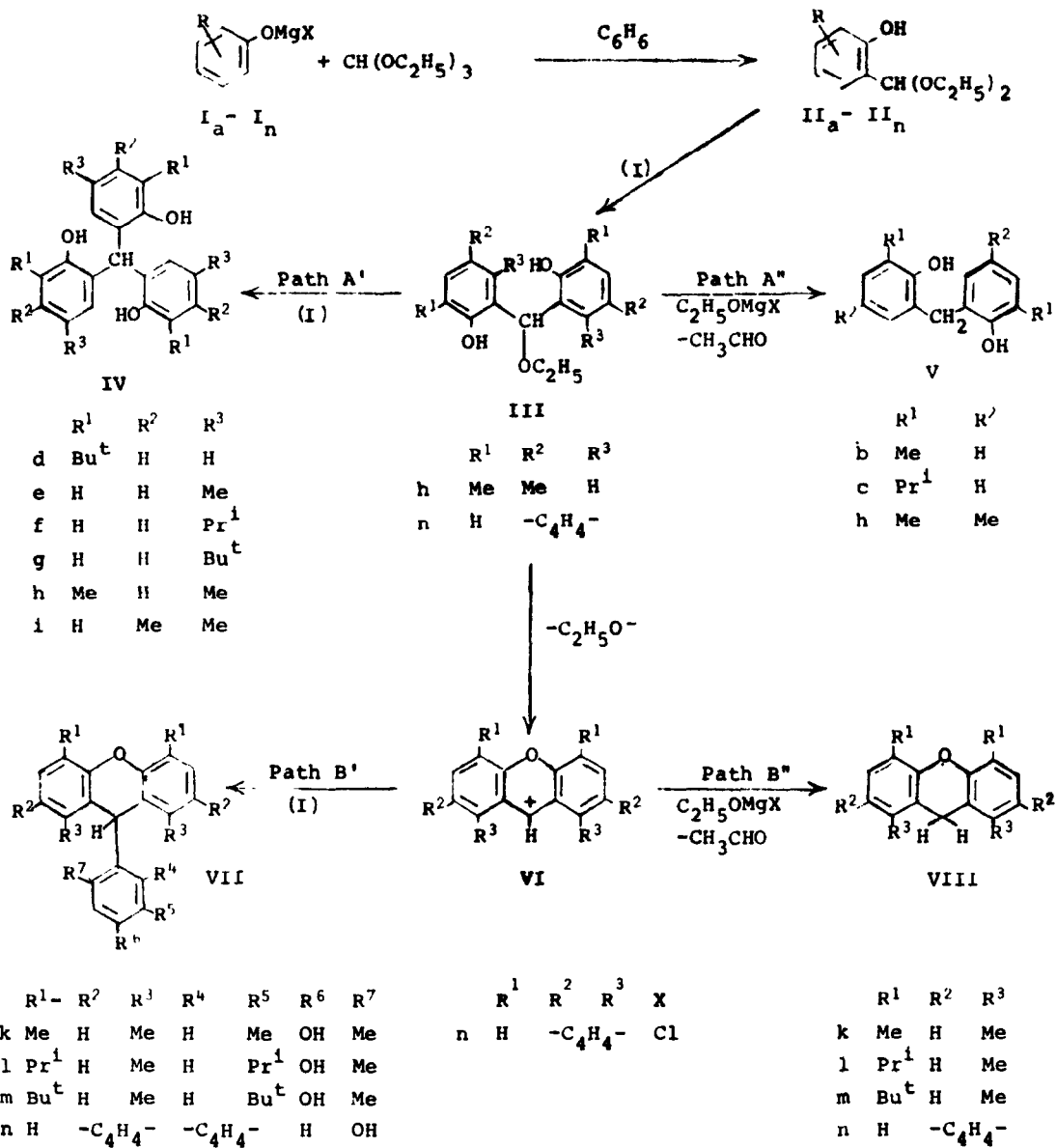
Now, it has been possible to hypothesize the following reaction pathway: a first C-regiospecific attack of triethyl orthoformate at the phenolic system (I) giving 2-hydroxyaryl-1-carboxyaldehyde diethylacetals (II) isolable during the reaction; II is a common intermediate in these reactions and reacts again with the aryloxymagnesiumhalides (I) to form the ethers (III) (reactions of I_h and I_n afford III_h and III_n).

Moreover, we have proved that (II_n) reacts with (I_n) giving (III_n) (benzene at r.t) or ($VIII_n$) and (VII_n) (refluxing benzene).

Analogously (II_d) and (I_d) lead to (IV_d) in good yields.

Compound (II) represents the branching point in the process which follows different paths, depending on the position of the alkyl-substituents on the phenolic substrate. The following competitive pathways are observed:
Paths A : intermediate (III) from monoalkylphenoxy magnesiumhalides (I_b , I_c , I_d , I_e , I_f , and I_g) and from dialkylphenols (I_h and I_i) leads to 2,2',2"-trihydroxytriphenylmethanes (IV) according to a C-regiospecific reaction with (1) (path A'), or to 2,2'-dihydroxydiphenylmethanes (V) by an ox-redox process with ethoxymagnesiumhalide⁵ (Path A"). In fact, we have proved that

Scheme



TABLE

Reactions of alkylphenoxymagnesiumbromides (I) with triethylorthoformate. 1 : 1 mole ratio of phenoxy salt to orthoformate; conc. 0.2 mole/litre (benzene as solvent).

Starting Phenol (I)	Reaction conditions ^{††}	% yield products (m.p.) [§]							
		II	III	IV	V	VII	VIII		
a phenol	B, 80°, 1 hr.	a 10							
b 2-Me	B, 60°, 24 hr.	b 2			b 42 (120°)				
c 2-Pr ⁱ	B, 45°, 24 hr.	c 4			c 50 (102°)				
d 2-Bu ^t	B, 80°, 1 hr.	d 2		d 83 (218°)					
e 4-Me	B, 80°, 12 hr.	e 1		e 23 (170°)					
f 4-Pr ⁱ	B, 80°, 12 hr.	f 4		f 70 (118°)					
g 4-Bu ^t	B, 80°, 12 hr.	g 8		g 64 (137°)					
h 2,4-Me	B, 80°, 10 hr.	h 8	h 55 (oil)	h 5 (260°)	h 30 (148°)				
h 2,4-Me	B, 80°, 36 hr.	h 3		h 12 (160°)	h 85 (148°)				
i 3,4-Me	B, 80°, 12 hr.	i 5		i 85 (246°)					
k 2,5-Me	B, 80°, 12 hr.	k 4				k 34 (242°)	k 45 (172°)		
l 2-Pr ⁱ -5-Me	B, 80°, 12 hr.	l 2				l 35 (234°)	l 44 (169°)		
m 2-Bu ^t -5-Me	B, 80°, 10 hr.	m 3				m 5 (250°)	m 70 (219°)		
n 8-naphtol	E, 20°, 12 hr.	n 20	n 70 (180°)						
n 8-naphtol	E, 35°, 3 hr.	n 10	n 85 (180°)						
n 8-naphtol	B, 20°, 3 hr.	n 10	n 70 (180°)						
n 8-naphtol	B, 80°, 12 hr.	n 5	n			n 20 (276°)	n 70 (205°)		

[†]Analogous results were observed with magnesiumchlorides and iodides.

^{††}B = dry benzene; E = dry diethylether.

[§]All structures are based on analytical, mass spectral, n.m.r., i.r., and u.v. data; (III) were identified, after hydrolysis to 2-hydroxycarboxyaldehyde, by comparison with authentic materials; m, ps are uncorrected; Yields, were determined by g.l.c.

(III_h) reacts in refluxing benzene with (I_h) to give (IV_h), while, in the same conditions, with an equimolecular amount of ethoxymagnesiumhalide gives (V_h) and acetaldehyde.

Paths B: intermediate (III) from phenoxymagnesiumhalides (I_k, I_l, I_m, and I_n), which bear a substituent near the position of attack, gives a new type of aromatic cyclization leading to xanthenes systems,⁶ via xanthilium ion (VI). Hydroxyarylxanthenes (VII) are obtained by an electrophilic attack of (VI) on (I) (Path B') and xanthenes (VIII) by an ox-redox process involving (VI) and ethoxymagnesiumhalide (Path B"). In agreement with this hypothesis (III_n) reacts with (I_n) in refluxing benzene to afford (VII_n), while with ethoxymagnesiumhalide, under the same conditions forms (VIII_n) and acetaldehyde. Furthermore, (VI_n)⁷ gives (VII_n) by reaction with (I_n) in refluxing benzene and (VIII_n) by reduction with ethoxymagnesiumbromide.

References and footnotes

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- ³B. Cardillo, G. Casnati e A. Pochini, *Chimica e Industria*, **49**, 630 (1967).
- ⁴A. Hassner and F. Boerwinkle, *J. Amer. Chem. Soc.*, **90**, 216 (1968).
- ⁵It is known that alcohols reduce, in acidic conditions, diphenylcarbinols and diphenylalkylethers to diphenylmethane derivatives via a carbonium ion intermediate. G. A. Olah and P. von R. Schleyer "Carbonium Ions", Vol. II, Wiley Interscience Publ., 1970, p. 482.
- ⁶Synthesis of xanthenes derivatives by cyclization of 2,2'-dihydroxydiphenylalkanes or 2,2'-dihydroxytriphenylalkanes occurs in poor yields under drastic conditions (by pyrolysis or in acidic media at high temperature). R. D. Elderfield, "Heterocyclic Compounds", John Wiley & Sons Inc., New York, 1951, chap. 13 and references therein.
- ⁷(VI_n) was obtained by reaction of (III_n) in diethylether with gaseous hydrochloric acid as orange needles. The utilization of these methods for general synthesis of xanthilium salts is in progress.